Anaesthesia and Beckwith - Weideman Syndrome

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Synopsis of patient: A 15 hour old, 4.2 kg male presents for closure of a large exomphalos. He was delivered by C-section for foetal distress after a prolonged labour at a peripheral hospital. Apgars were recorded as 6 and 8. His mother was an unmarried primigravida who attended antenatal clinic on one occasion. Meconium aspiration was suspected at birth. Preoperative assessment revealed a large term baby with features of Beckwith-Weideman syndrome - a large tongue; a faint naevus on the forehead; and a skin crease on the ear lobe. Assessment of the liver and spleen was difficult in view of the large omphalocoele (5x6cm). The exomphalos was stained by the meconium in utero. He was tachypnoeic but the chest was clear. There was a 2/6 ejection systolic murmur at the left sternal border. Chest xray was normal apart from mild cardiomegaly. Blood sugar on admission was 1.2 mmol.l ; electrolytes were within normal limits. Haemoglobin was 17gm. (Hct 55)

Beckwith-Weideman syndrome

Beckwith-Weideman syndrome (BWS) is an autosomal dominant syndrome with variable expressivity[1] and is characterised by abdominal wall defects, (usually exomphalos), macroglossia, and gigantism often associated with visceromegaly, adrenocortical cytomegaly, and dysplasia of the renal medulla (Table 1). The syndrome was first described by John Bruce Beckwith, a paediatric pathologist in Seattle (but South African born!) in 1963[2]. Hans Rudolf Weidemann, professor in paediatrics at Kiel University (Germany), also described the syndrome at much the same time[3]. More recently the syndrome has become known as the EMG syndrome: exomphalos - macroglossia - gigantism[1].

Most cases occur sporadically and the incidence is reported to be in the order of 1:14000 births[1,4]. 23% of 123 exomphalos presenting at King Edward VIII hospital in Durban over a 12 year period had features of BWS.(unpublished data). Family studies indicate linkage of the BWS to the marker 11p15.5 and the IGF-II gene located at that locus. The cellular and tissue overgrowth may be due to an underexpression of a negative regulator protein for cell proliferation (p57 gene) and overexpression of an insulin-like growth factor gene (IGF-II)[5]. Increased levels of IGF-II mRNA have been detected in numerous tumours associated with BWS such as nephroblastomas, neurblastomas, rhabdomyosarcomas, and adrenocortical carcinomas.[4] Abnormalities of chromosome 11,[6] including Trisomy 11p15,[7] have been associated with BWS.

The time dependant nature of many abnormalities in BWS can challenge the anaesthesiologist at various stages in the child's life[8,9,10]. Macroglossia and hypoglycaemic episodes seen in the neonatal period may disappear with growth and time. Gigantism, microcephaly, mental retardation secondary to hypoglycemia in the neonatal period, or cor pulmonale secondary to upper airway obstruction may develop later in childhood.

The typical facial features include macroglossia(Fig 1); a capillary haem-angioma on the central forehead, often described as flame shaped, flammeus naevus; and linear creases on the earlobe(Fig 2). Indentations of the external helix may also be seen. Other less common features described in older children include microcephaly, prognathism, malocclusion and relative exophthalmos.

At laryngoscopy, macroglossia may make visualisation of the cords difficult. Macroglossia, may also cause significant upper airway ob-

Table 1: Spectrum of clinical feature[4,13].

Clinical Characteristic	*Percentage*
Prematurity	50%
Macroglossia	92%
Abdominal wall defect	68%
High birth weight	53%
Facial abnormality	52%
Visceromegaly	50%
Hypoglycemia	30-50%
Persistent hypoglycemia	<5%
Renal anomalies	Up to 59%
Family history	50%
Incidence tumours	7.5 - 10% (up to 21%)

Figure 1: Facial features of a neonate with BWS

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Figure 2: Typical creases on the ear lobe.

struction, which may be acute or chronic. Acute airway obstruction may lead to alveolar hypoventilation and subsequent hypoxia and hypercapnia. If this becomes chronic, cor pulmonale may result[11]. Tracheostomy may be indicated in some cases. Anterior tongue reduction may then be considered provided that other more common causes of upper airway obstruction have been excluded such enlarged tonsils and adenoids[11]. Other indications for anterior tongue reduction include malocclusion, difficulties with deglutition, articulation errors and cosmesis.[11]

A variety of other cardiac anomalies have been described. These include atrial septal defects, ventricular septal defects, patent ductus arteriosus, tetralogy and hypoplastic left ventricle or idiopathic cardiomegaly[12]. The idiopathic cardiomegaly is not usually associated with cardiorespiratory symptoms and may regress by six months of age. It has been attributed to hypoglycaemia or visceromegaly.[12] Cor pulmonale may occur secondarily to upper airway obstruction.

Visceromegaly may involve the kidneys, liver, pancreas, adrenals and gonads. The renal medulla may be dysplastic and hypercalciuria has been described. There is increased risk of childhood malignancy and a strong association with Wilms tumour. Other intra-abdominal malignancies that have been associated with BWS include hepatoblastoma, adrenocortical carcinoma, neuoroblastoma, rhabomyosarcoma, and gonadoblastoma. Children with BWS should be screened regularly for at least 4-6 years to detect the development of these embryonal tumours cancers early.

Renal abnormalities may occur in up to 59% of patients with BWS. [13] Neonatal nephromegaly may regress by four months but structural abnormalities of the renal medulla and collecting system may present in 15-25% of cases[14]. Abnormalities of the renal medulla may be associated with nephrocalcinosis and hypercalciuria[13]. Infants with persistent nephromegaly are considered to be at risk of developing Wilms tumour.[15]

Neonatal hypoglycaemia is common (30-50%)[5] and must be treated timeously in the neonatal period to prevent permanent neurological damage. It is secondary to pancreatic cell hyperplasia and the resultant hyperinsulinaemia. Hypoglycaemia may be mild or severe and is usually responsive to corticosteroids. Diazoxide, glucagon, adrenaline and other hyperglycaemic medications may need to be added in various combinations to correct resistant cases. The hypoglycaemia usually resolves spontaneously by the end of the fourth month. Less than 5% will have hypoglycemia beyond the neonatal period[5] but if it persists, or is very severe, nesidioblastosis should be suspected. Continuous glucose infusions may be required to maintain normoglycemia until a total or partial pancreatectomy can be performed.

Figure 3: Large abdominal wall defect (Exomphalos major) prior to surgery.

The majority of infants with hypoglycemia are asymptomatic in the neonatal period. Diagnosis can be difficult and all neonates with exomphalos should have a blood glucose checked. Early detection is important and may prevent long term neurological complications. Antenatal diagnosis of BWS is difficult[16,17]. Indicators that should alert investigators include polyhydramnios, placentomegaly, enlarged kidneys, increased abdominal circumference and rapid growth from 24-36 week gestation.[17,18]

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